REMARKS

Further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested.

Claim 25 has been rejected under 35 U.S.C. 112, first paragraph for allegedly lacking written description. Applicants respectfully traverse.

The Examiner's rejection is confusing because claim 25 is not drawn to sequences having 80% homology with SEQ ID NO:38 that can bind to SEQ ID NO:38. Claim 25 is drawn to a polypeptide from a phage display that can bind to the polypeptide according to claim 23 (i.e., SEQ ID NO:38). It is routine in the art to use phage display to identify molecules that, e.g., bind to other molecules.

Claims 24 and 26, which recite a % homology, also include an associated functional activity. One of ordinary skill in the art, using conventional techniques in modern molecular biology, would be able to construct polypeptides having sequences which are 80% or 90% homologous to the polypeptide of SEQ ID NO:38 and possess the associated function identified as a human mRNA putatively prenylated protein, as described for the encoding SEQ ID NO:16. See e.g., the specification at page 55. Also, review of the expression data collected in a Northern blot analysis for SEQ ID NO:16 clearly indicates it as being expressed in significantly higher levels in uterus myometrium tumor tissue as compared to normal uterus myometrium tissue expression (see specification at page 33). One of ordinary skill in the art, using conventional techniques or assays would be able to ascertain that the polypeptides having 80 or 90% homology have the associated functional activity.

Thus, the rejection of the claims under §112, first paragraph, should be withdrawn.

Claims 23-26 have been rejected under § 112, first paragraph, and 35 U.S.C. § 101 because the claimed invention allegedly lacks patentable utility. Applicants respectfully traverse this rejection.

It is general knowledge in the art that cancer in general is related to the up regulation of certain proteins in tumor cells. This is evident from the state of the art disclosing polypeptides or proteins which are upregulated or essentially unaffected in tumor cells.

As explained in the specification, the claimed polypeptides are coded for by a nucleic acid which is overexpressed in uterus myometrium tumor tissue and therefore can be used, e.g., as diagnostic markers and disease targets. SEQ ID NO:38 which is coded for by SEQ ID NO:16 (page 57 of the specification) is shown on page 33 as being expressed at higher levels in uterus myometrium tumor tissue as compared to normal uterus myometrium tissue. As indicated on Page 468 of the attached page from the Molecular Biology of the Cell, "transcription (transcriptional control) usually predominates" in "the pathway from RNA to protein," leading to the reasonable expectation that overexpression of the RNA would lead to overexpression of the corresponding protein. Thus, polypeptides of SEQ ID NO:38 would be useful as diagnostic markers for uterus myometrium cancer. This utility is adequate to meet the requirements of § 101. See, e.g., *Utility Guidelines*, Pages 69-70, where a marker for cancer is described as having a well-established utility.

The fact that polypeptides of SEQ ID NO:38 are overexpressed in tumor cells also provides a reasonable basis for their use as pharmaceutical agents, e.g., to generate antibodies *in vivo* to tumor tissue (i.e., vaccine immunotherapy). There are a number of antibody-based products that are in therapeutic use which are targeted at polypeptides expressed in tumor tissue, including, e.g., Herceptin® (Trastuzumab) and Rituxan® (Rituximab). Instead of the antibody, the target polypeptide can be administered to induce the antibodies *in situ* in the subject to be treated. Given the data showing overexpression of the polypeptide coupled with the state of the art, there is no scientific reason to doubt the validity of the asserted utility.

Therefore, applicants request withdrawal of this rejection.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned attorney or agent concerning such questions so that prosecution of this application may be expedited.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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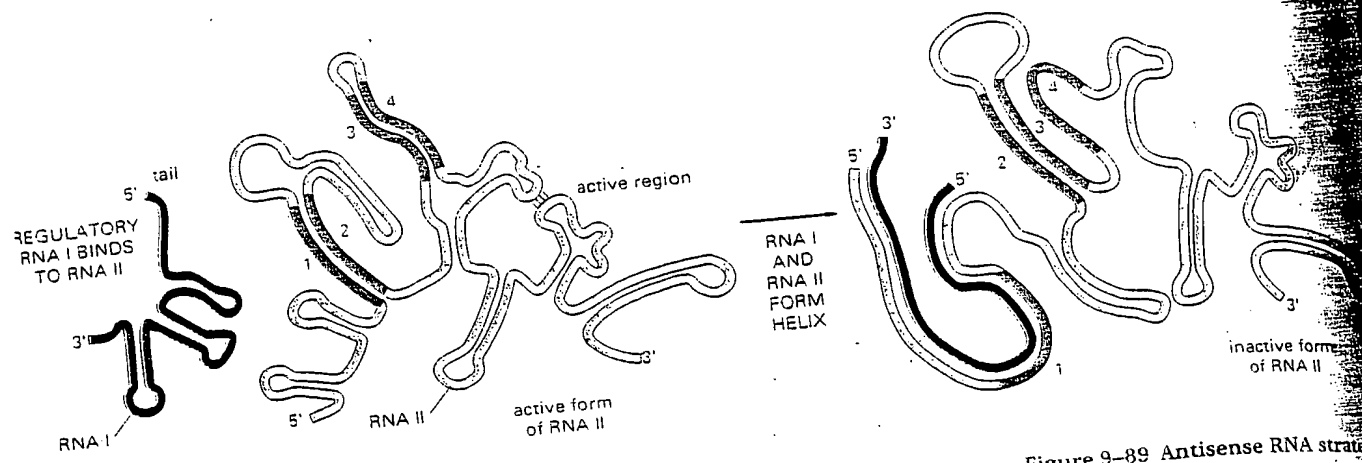

Figure 9–89 Antisense RNA strate... for regulating plasmid numbers in bacteria. A regulatory interaction between two RNA molecules maintains a constant plasmid copy number in the ColE1 family of bacterial DNA plasmids. RNA I (abou... 100 nucleotides long) is a regulatory RNA that inhibits the activity of RNA II (about 500 nucleotides long), which normally helps initiate plasmid DNA replication. The concentration of RNA I increases in proportion to the number of plasmid DNA molecules in the cell, so that as plasmid numbers increase, plasmid replication is inhibited. RNA I is complementary in sequence to the 5′ end of RNA II. In RNA II sequence 2 is complementary to both sequence 1 and sequence 3, and it is displaced from one to the other by the binding of RNA I; RNA I thereby alters the conformation of sequence 4, inactivating RNA II. (After H. Masukata and J. Tomizawa, *Cell* 44:125–136, 1986.)

accomplished by specialized RNA-binding proteins. In other cases, however, the recognition of specific RNA sequences is carried out by other RNA molecules, which use complementary RNA-RNA base-pairing as part of their recognition mechanism. RNA-RNA pairings, for example, are known to play a central part in translation, in RNA splicing, in several other forms of RNA processing, and in the RNA editing that occurs in trypanosomes. In attempting to dissect posttranscriptional mechanisms, we have largely entered an RNA world.

RNA molecules also have other regulatory roles in cells. The *antisense RNA* strategy for experimentally manipulating cells so that they fail to express a particular gene (see p. 326) mimics a normal mechanism that is known to regulate the expression of a few selected genes in bacteria and may be used much more widely than is now realized. A well-understood example of this kind of mechanism provides a feedback control on the initiation of DNA replication for a large family of bacterial DNA plasmids. The control system limits the number of copies of the plasmid made in the cell, thereby preventing the plasmid from killing its host cell by overreplicating (Figure 9–89).

Studies of RNA-catalyzed reactions are of special interest from an evolutionary perspective. As discussed in Chapter 1, the first cells are thought to have lacked DNA and may have contained very few, if any, proteins. Many of the RNA-catalyzed reactions in present-day cells seem to represent molecular fossils—descendants of the complex network of RNA-mediated reactions that are presumed to have dominated cell metabolism more than 3.5 billion years ago. Recombinant DNA technology has allowed large amounts of pure RNAs of any sequence to be produced *in vitro* with purified RNA polymerases (see Figure 7–36), making it possible to study the detailed chemistry of RNA-catalyzed reactions. From an understanding of many such reactions, biologists hope to be able to trace the path by which a living cell first evolved.

Summary

Many steps in the pathway from RNA to protein are regulated by cells to control gene expression. Most genes are thought to be regulated at multiple levels, although control of the initiation of transcription (transcriptional control) usually predominates. Some genes, however, are transcribed at a constant level and turned on and off solely by posttranscriptional regulatory processes. These processes include (1) attenuation of the RNA transcript by its premature termination, (2) alternative RNA splice-site selection, (3) control of 3′-end formation by cleavage and poly-A addition, (4) control of transport from the nucleus to the cytosol, (5) localization of mRNAs to particular parts of the cell, (6) RNA editing, (7) control of translational initiation, (8) regulated mRNA degradation, and (9) translational recoding. Most of these control processes require the recognition of specific sequences or structures in the RNA molecule being regulated. This recognition can be accomplished by either a regulatory protein or a regulatory RNA molecule.

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Front cover: The photograph shows a rat nerve cell in culture. It is labeled (*yellow*) with a fluorescent antibody that stains its cell body and dendritic processes. Nerve terminals (*green*) from other neurons (not visible), which have made synapses on the cell, are labeled with a different antibody. (Courtesy of Olaf Mundigl and Pietro de Camilli.)

Dedication page: Gavin Borden, late president of Garland Publishing, weathered in during his mid-1980s climb near Mount McKinley with MBoC author Bruce Alberts and famous mountaineer guide Mugs Stump (1940–1992).

Back cover: The authors, in alphabetical order, crossing Abbey Road in London on their way to lunch. Much of this third edition was written in a house just around the corner. (Photograph by Richard Olivier.)